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SALVARSAN IN LEPROSY

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SALVARSAN IN LEPROSY.*

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*(Studies from the Laboratories of Tropical Medicine and Hygiene
under the direction of Creighton Wellman, Medical Department,
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In a preliminary note¹ were discussed the clinical findings in a series of seven lepers of whom five received treatment with salvarsan and two were injected at the same time with normal salt solution and observed as controls.

There was a gain in weight and in the appearance of the superficial lesions, notably of the throat and skin in the patients treated. In none of the cases was there any clinical evidence that the bacilli in the tissues were destroyed or that their activity was impaired. The conclusions arrived at from a physical examination of the series of patients were that no immediate injurious effects follow from the administration of the drug in cases which are not too far advanced, and that in such cases some improvement may be expected.

At the time the experiments were carried out careful laboratory findings were recorded along with the clinical notes, and it is the purpose of the present paper to present these laboratory findings.

*Specimens, photographs, and lantern slides illustrating this paper were exhibited before the American Society of Tropical Medicine and the Pathological Section of the American Medical Association, Atlantic City, June 4-7, 1912.

¹Preliminary Report on the Experimental Administration of Salvarsan in Some Cases of Leprosy, read at the eighth annual meeting of the American Society of Tropical Medicine, New Orleans, May 18, 19, 1911, *Southern Medical Journal*, iv, 11, pp. 849-851, December, 1911.



METHOD OF STUDY.

The following were examined as hereafter described, one set of specimens being taken one week

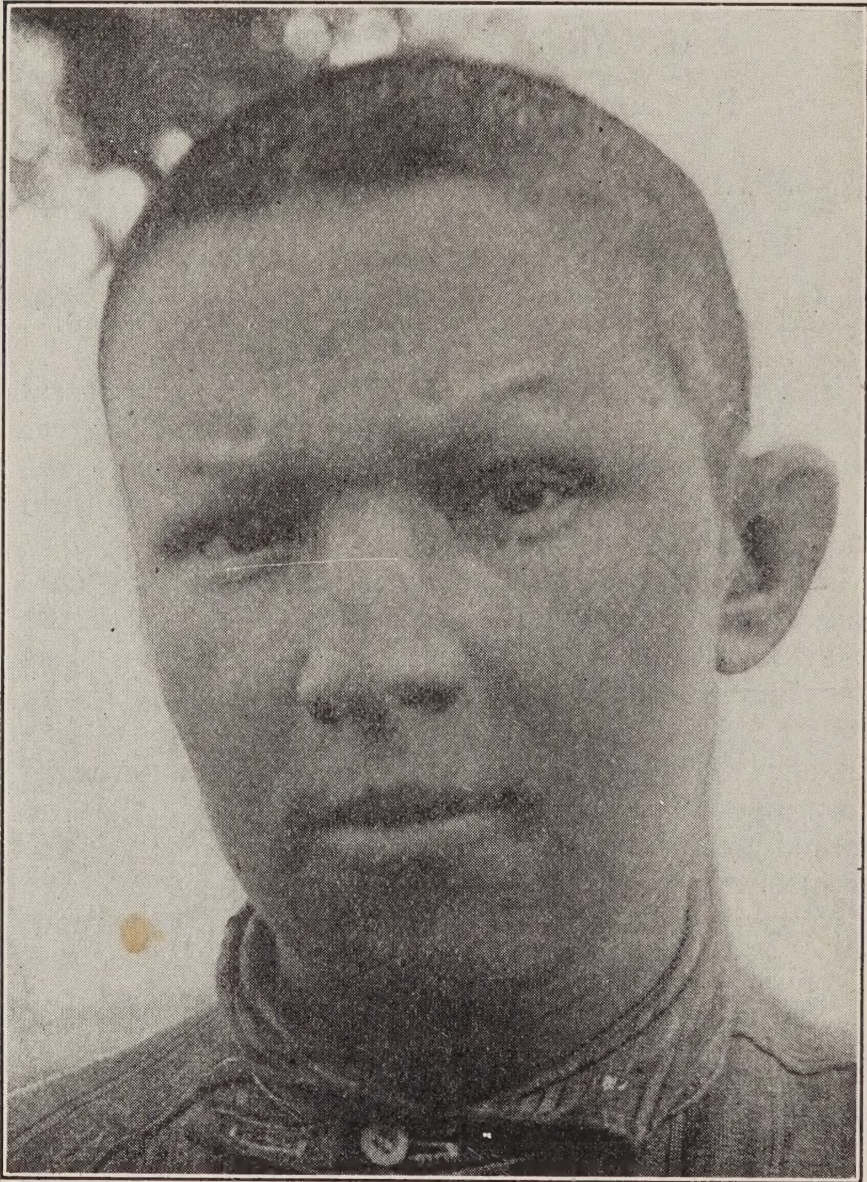


FIG. 1.—Photograph, Case 1.

before the administration of salvarsan and the other specimens being taken seven weeks after the administration of salvarsan:

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1. Smears of nasal mucus.
2. Blood smears.
3. Urine.

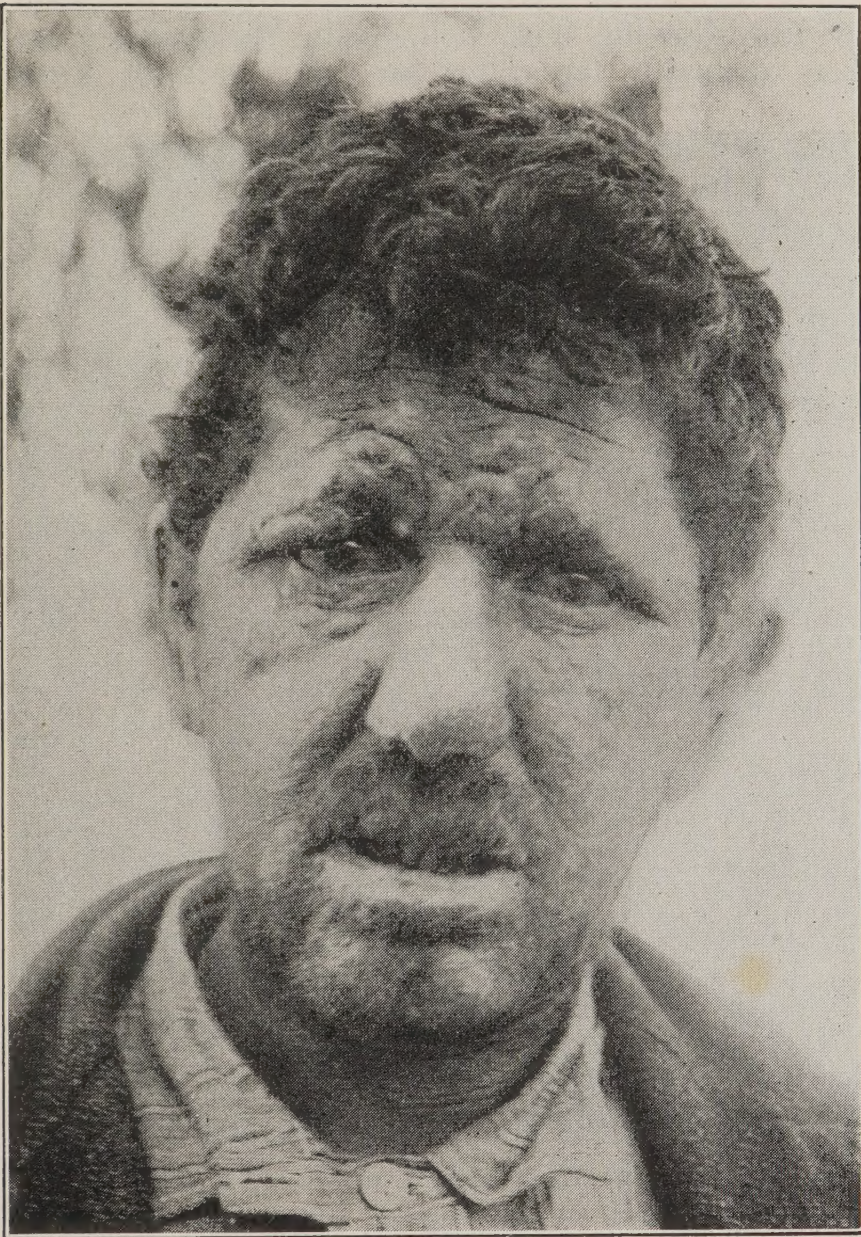


FIG 2, a.—Photograph, Case 2.

4. Excised leprous nodules.
5. Feces.

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1. All smears from the nose were fixed with heat at the time of taking. Immediately after the smears were stained with freshly prepared Ziehl Neelsen carbol fuchsin for three minutes, warming the stain but not allowing it to boil. The specimens were then washed in tap water for a few seconds, after

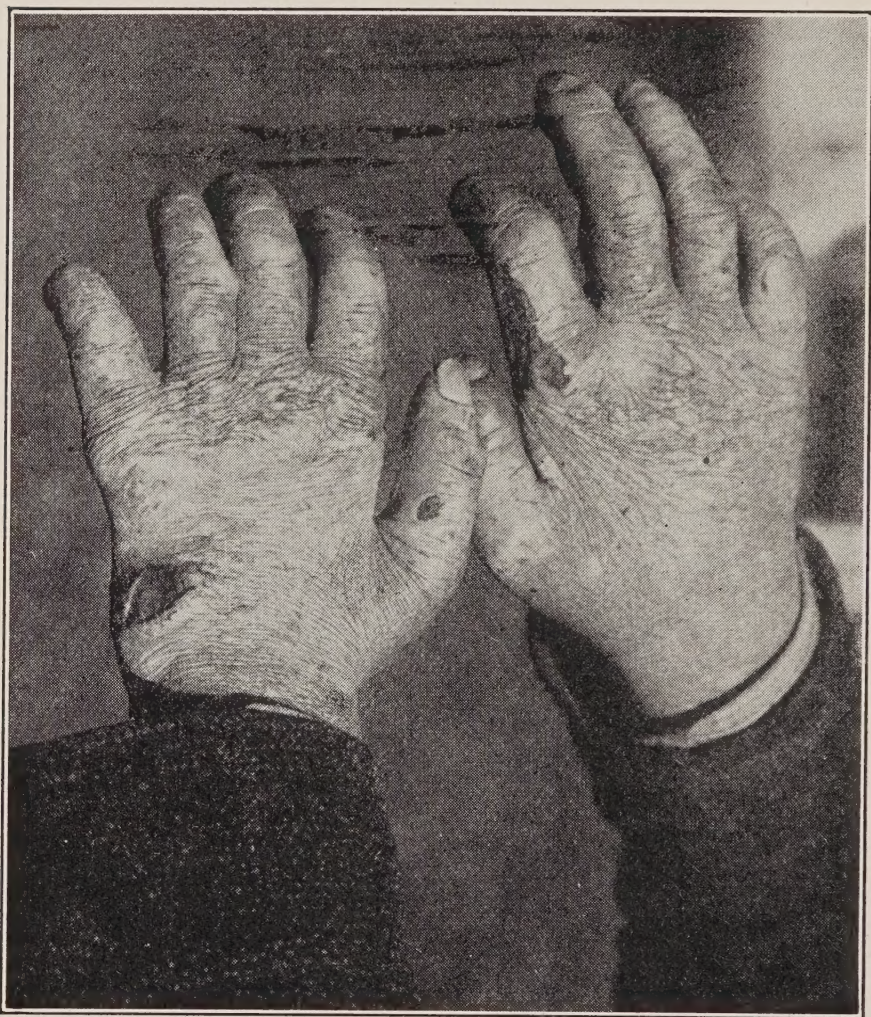


FIG. 2, b.—Hands in Case 2.

which they were covered with a twenty per cent. solution of sulphuric acid two or three times, and again washed in tap water for less than one minute. Then the smears were covered with ninety-five per cent. ethyl alcohol for thirty seconds and washed in

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water to remove alcohol. Finally they were counterstained with Löffler's methylene blue for one minute, dried, and mounted.

The following table shows the result of an examination of these smears:

No.	Name	Time	Findings	Remarks
1.	F. Correa.....	Before		Early case.
	F. Correa.....	After		Clinically much improved.
2.	T. Smith.....	Before		Moderately advanced case.
	T. Smith.....	After		Clinically much improved.
3.	Lee Sing.....	Before	B. lepræ	Very advanced case
	Lee Sing.....	After	?	Died from accidental burns.
4.	O. Shibuya....	Before	B. lepræ	Control.
	O. Shibuya....	After	B. lepræ	Grew much worse and died.
5.	Joe Correa....	Before	B. lepræ	Advanced case.
	Joe Correa....	After	B. lepræ	Clinically improved.
6.	John Hoy.....	Before		Control, anesthetic type
	John Hoy.....	After		
7.	Mary Delgado..	Before	B. lepræ	Early case.
	Mary Delgado..	After		Clinically much improved.

It will be seen from this table that nothing of note can be deduced from the comparison of nasal smears taken from these cases before and after treatment. In case seven the bacilli disappeared from the nose after treatment.

2. In staining the blood smears Wright's stain was used exclusively. Talqvist's scale was employed in a rough estimation of the percentage of hemoglobin.

The first table, on page 6, shows the result of an examination of these specimens of blood.

It will be noted that these examinations throw little light on the question of improvement under salvarsan. Three cases showed increase in number of red cells.

3. All specimens of urine examined were passed in the morning after breakfast was eaten and were examined an hour later. In testing for albumin Heller's cold nitric acid, and the heat test with the later addition of acetic acid, were both used in all examinations. No quantitative estimation was made. Fehling's test was used for sugar.

Nothing of significance is suggested by the preceding table.

The second table, on page 6, shows the result of these examinations.

No.	Name.	Hemoglobin.		Differential count				Eosin. Per cent.	No. cells counted.	Remarks.
		Time.	Per cent.	Whites.	Neutro- philes. Per cent.	Large Monos. Per cent.	Small Monos. Per cent.			
1.	F. Correa	Before	95	18,600	48	7	43	2	500	
	F. Correa	After	95	15,600	56	8	34	2	500	
2.	T. Smith	Before	95	11,200	52	6	35	7	500	
	T. Smith	After	95	11,000	58	5	27	10	500	
3.	Lee Sing	Before	95	8,800	82	1	17	..	300	Counted two eosinophiles. Fatal from accidental burns.
	Lee Sing		..		..	..	..	..	...	
4.	O. Shibuya	Before	95	10,800	84	4	12	..	500	Control, counted one eosinophile.
	O. Shibuya	After	30	8,800	88	3	7	2	500	A few normoblasts found.
5.	Joe Correa	Before	85	16,000	48	2	38	12	500	
	Joe Correa	After	75	13,600	64	10	20	6	500	
6.	John Hoy	Before	95	9,000	65	6	28	1	300	Control.
	John Hoy	After	95	10,000	63	4	32	1	300	
7.	Mary Delgado	Before	95	12,000	57	6	37	..	500	Counted one eosinophile.
	Mary Delgado	After	95	9,000	62	5	32	1	500	

No.	Name.	Time.	Color.	Trans- parency.	Reaction.	Sp.gr.	Albumin	Sugar.	Casts.	Pus.	Blood.	Remarks.
1.	F. Correa....	Before	Amber	Slightly cloudy	Slightly acid	1.027	Large amount		A moderate amount hyaline			
	F. Correa....	After	Amber	Slightly cloudy	Slightly acid	1.020	Large amount		A moderate amount hyaline			
2.	T. Smith.....	Before	Amber	Clear	Slightly acid	1.025						
	T. Smith.....	After	Amber	Clear	Slightly acid	1.022						
3.	Lee Sing.....	Before	Yellowish	Cloudy	Acid	1.016	Trace		Many hyaline and dark granular amount	Small amount	A few cells	
	Lee Sing.....	Before	Reddish yellow	Very cloudy	Slightly alkaline	1.027	Large amount			Small amount	Large amount	Died from accident. Control.
5.	O. Shibuya....	Before	Brick dust	Very cloudy	Slightly alkaline	1.023						Died. Heavy sediment of amorphous urates
	Joe Correa....	After	Amber	Clear	Slightly acid	1.014						
6.	John Hoy....	Before	Reddish yellow	Cloudy	Slightly alkaline	1.021						Control. Moderate amount of amorphous urates.
	John Hoy....	After	Amber	Clear	Slightly acid	1.013	Faint trace					
7.	Mary Delgado.	Before	Dirty yellow	Very cloudy	Slightly acid	1.024	Small amount		Many hyaline and dark granular amount	Small amount	Small amount	
	Mary Delgado.	After	Light yellow	Slightly cloudy	Slightly acid	1.018	Very small amount		Fewer number of casts	Small amount		

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4. The excised nodules examined were stained after two methods, to show the histological architecture, and to reveal the numbers of contained



FIG. 3.—Photograph, Case 4.

Bacillus lepræ. The technique employed for these purposes was as follows:

a. For histological structure the specimens were placed immediately in ten per cent. solution of

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formaldehyde in normal sodium chloride solution. After twelve hours they were cut in proper sizes for mounting. They were then placed in another freshly prepared ten per cent. solution of formaldehyde in normal salt solution and put in the in-

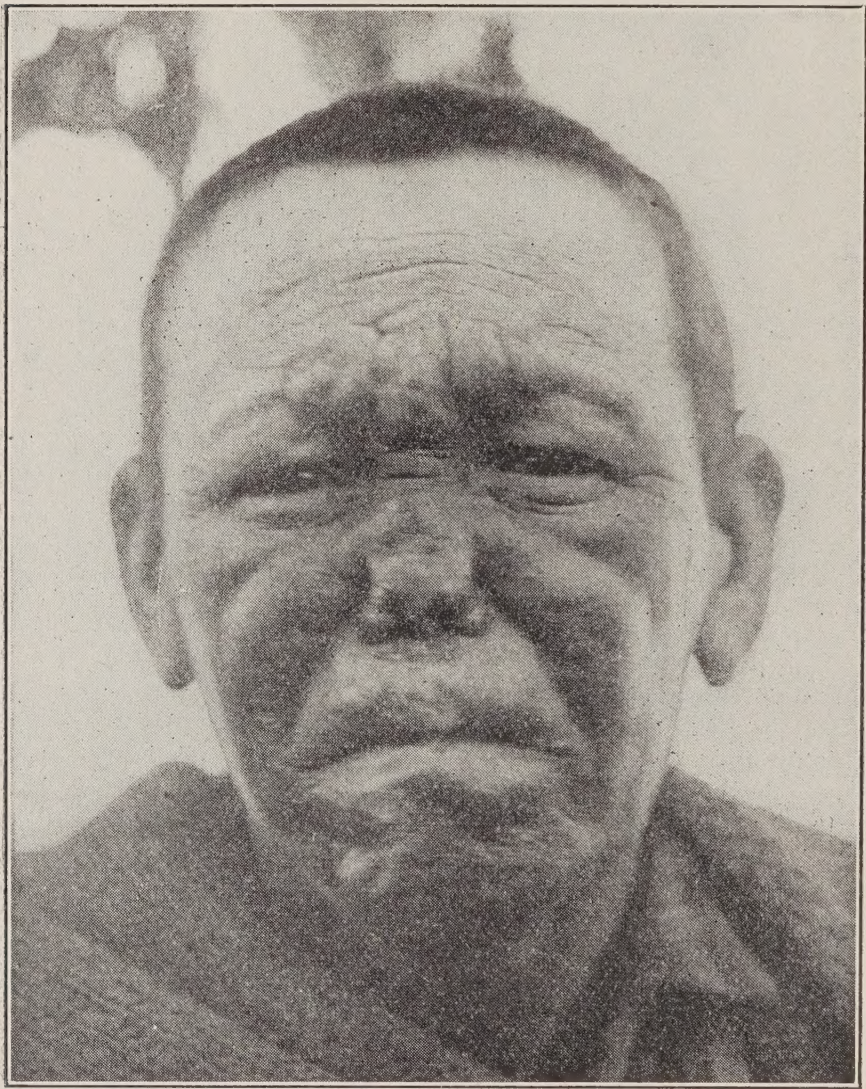


FIG. 4.—Photograph, Case 5.

cubator at 38° C. for twelve hours. After this the tissue was passed through the following manipulations:

- I. Seventy per cent. ethyl alcohol for twelve hours.

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2. Eighty per cent. ethyl alcohol for twenty-four hours.



FIG. 5.—Photograph, Case 6.

3. Ninety-five per cent. ethyl alcohol for twenty-four hours.

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4. Absolute ethyl alcohol for twenty-four hours.
5. Absolute ethyl alcohol and ether, equal parts, for twenty-four hours.
6. Xylol until clear (usually about one half hour).
7. Xylol and paraffin (melting point 43° C.), equal parts, for one half hour.
8. Paraffin (melting point 43° C.) for two hours at 55° C.
9. Paraffin (melting point 54° C.) for one hour at 55° C.
10. Mounted on blocks and thrown into cold water for five minutes.

The sections were then cut, fastened on slides, and stained for three minutes in Delafield's hematoxylin for the nuclear staining, after which they were counterstained with a dilute solution of eosin, cleared in xylol, and mounted in balsam.

The following table shows the results of an examination of these sections:

No.	Name.	Time.	Histological architecture.	Remarks.
1.	F. Correa	Before	Typical active lepra lesion, giant cells, and globi.	
	F. Correa	After	Epithelioid and plasma cells, resolution fairly well advanced.	
2.	F. Smith	Before	Typical active lepra lesion.	
	F. Smith	After	Some evidence of inflammation, polymorphonuclear leucocytes, a few plasma and epithelioid cells.	
3.	Lee Sing	Before	Typical lepra lesion plus some beginning necrosis.	
	Lee Sing	After	?	Died from result of accident.
4.	O. Shibuya	Before	Typical lepra lesion.	Control.
	O. Shibuya	After	Inflammation and necrosis.	Died.
5.	Joe Correa	Before	Typical lepra lesion.	
	Joe Correa	After	Giant cells and a few globi persist, but with some evidences of resolution. Plasma and epithelioid cells, etc.	
6.	John Hoy	Before	Atypical lesion, but a few giant cells, no globi nor discrete bacilli.	Control.
	John Hoy	After	Unchanged.	
7.	Mary Delgado	Before	Typical lepra lesion.	
	Mary Delgado	After	Almost complete resolution, lesion essentially a cicatrix.	



FIG. 6.—Photomicrograph of active lepra lesion, before treatment, low power. Note thinning and smoothing of skin.

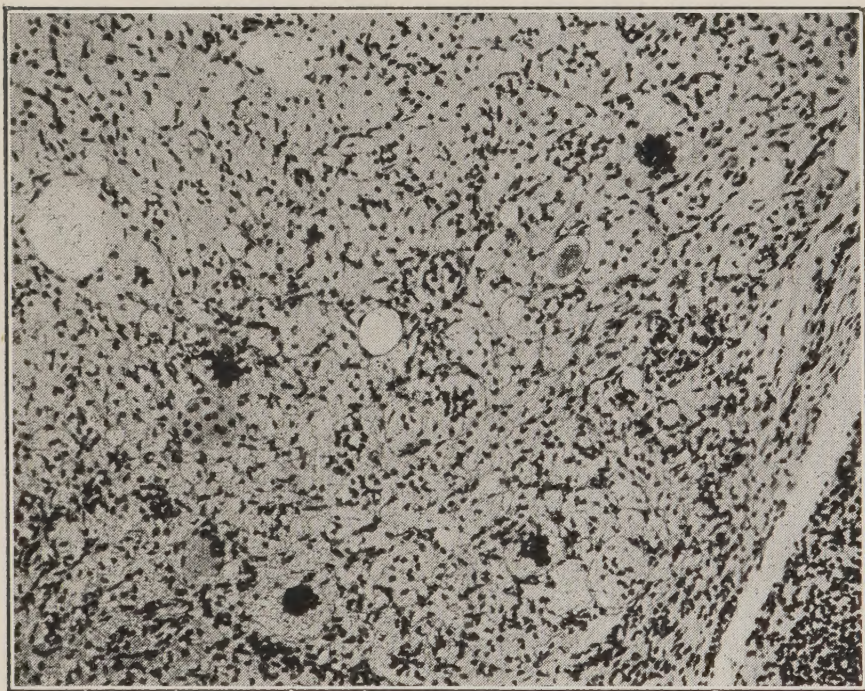


FIG. 7.—Higher power of lepra lesion, showing globi and giant cells. The open spaces are where globi of bacilli have dropped out of the section.

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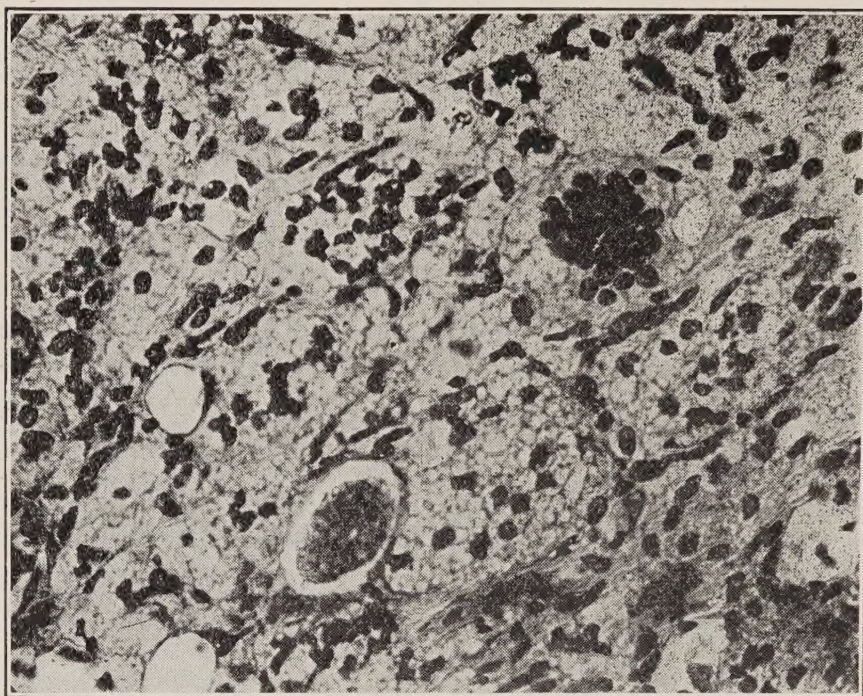


FIG. 8.—Very high magnification of lepra lesion, showing in detail a globus and a giant cell with many nuclei.

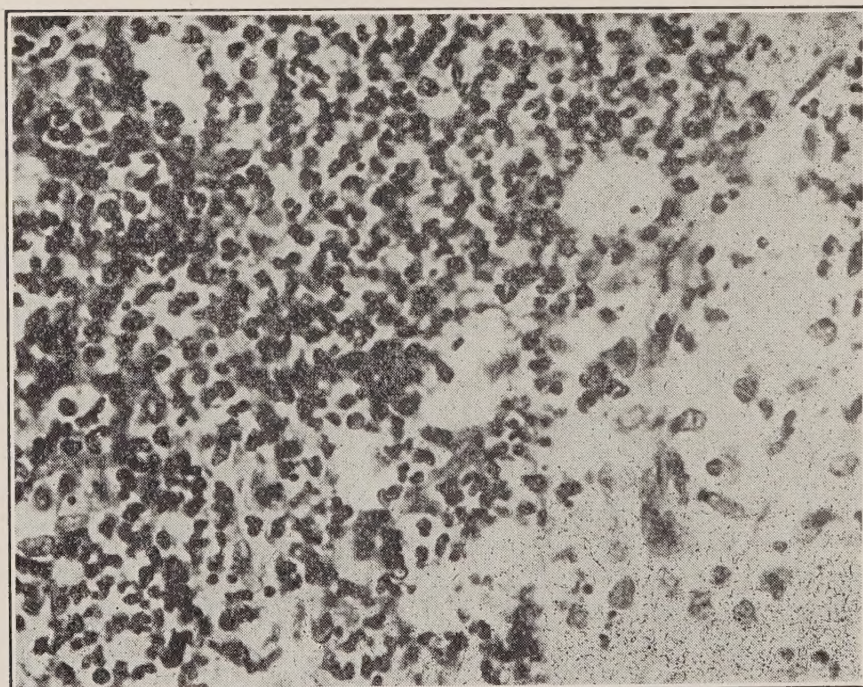


FIG. 9.—Lepra lesion after treatment. Giant cells are still present, but stain very faintly, numerous polymorphonuclear leucocytes are seen, with a few epithelioid cells.

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b. The technique used in staining sections for bacilli was as follows: The sections were fixed, hardened, and mounted on blocks in the same manner as those intended for histological sections, then they were stained with cold Ziehl Neelsen for twenty-four hours, and afterward treated the same as the smears of nasal mucus, and finally counter-stained.

The following table shows the results of an examination of these sections:

No.	Name.	Time.	<i>B. lepræ.</i>	Remarks.
1.	F. Correa	Before	Positive.	
	F. Correa	After	Negative.	
2.	T. Smith	Before	Positive.	
	T. Smith	After	Positive.	Number greatly diminished, very few found.
3.	Lee Sing	Before	Positive.	
	Lee Sing	After	?	Died from result of accident.
4.	O. Shibuya	Before	Positive.	Control.
	O. Shibuya	After	Positive.	Died.
5.	Joe Correa	Before	Positive.	
	Joe Correa	After	Positive.	
6.	John Hoy	Before	Negative.	Control.
	John Hoy	After	Negative.	
7.	Mary Delgado	Before	Positive.	
	Mary Delgado	After	Negative.	

This table shows the disappearance of *Bacillus lepræ* from the tissues in cases one and seven.

5. The feces were examined in the ordinary manner under low and high power.

The following table shows the results of the examination:

No.	Name.	Time.	Result of examination.	Remarks.
1.	F. Correa	Before	<i>N. americanus.</i>	
	F. Correa	After	<i>N. americanus.</i>	Number of ova unchanged.
2.	T. Smith	Before	<i>N. americanus.</i>	
	T. Smith	After	<i>N. americanus.</i>	Number of ova unchanged.
3.	Lee Sing	Before		
	Lee Sing	After		Died from accidental burns.
4.	O. Shibuya	Before		
	O. Shibuya	After		Died.
5.	Joe Correa	Before	<i>N. americanus.</i>	
	Joe Correa	After	<i>N. americanus.</i>	Number of ova unchanged.
6.	John Hoy	Before	<i>T. trichiris.</i>	Number of ova unchanged.
	John Hoy	After	<i>T. trichiris.</i>	Number of ova unchanged.
7.	Mary Delgado	Before		
	Mary Delgado	After		

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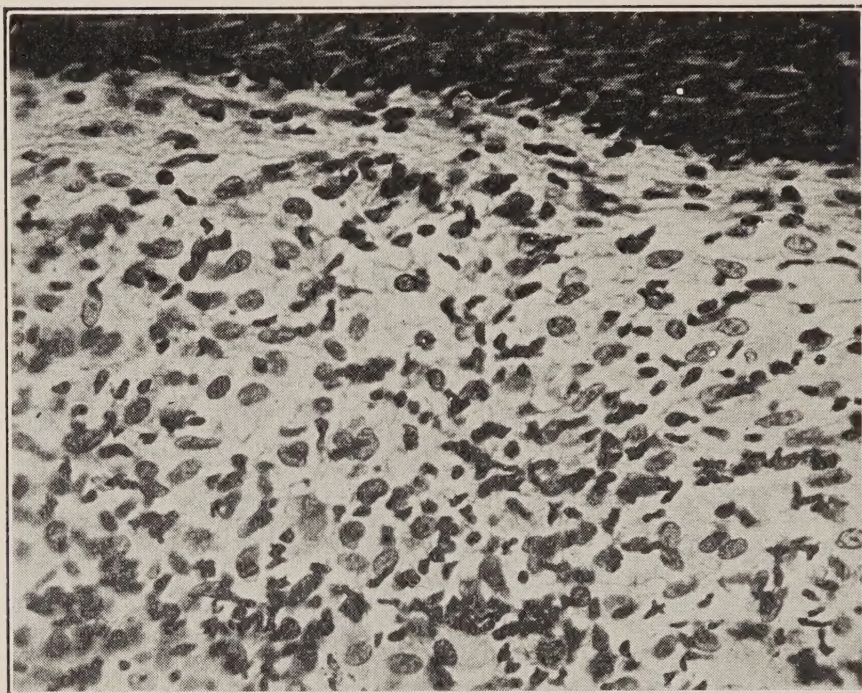


FIG. 10.—Another lesion after treatment, resolution well advanced, many epithelioid and plasma cells seen.



FIG. 11.—Another lesion after treatment (from Case 7), low power, showing resolution complete. The section is practically that of a cicatrix. Note normal appearance of skin.

SUMMARY AND CONCLUSIONS.

From the preceding study we find that the administration of salvarsan resulted in clinical improvement in four of the five patients treated.² The other case ended fatally from the result of accidental burns before observations could be completed. The two cases in which the disease was least advanced showed the best results. One of the controls remained unchanged in condition and the other grew steadily worse and finally died.

In case seven, *Bacillus lepræ* disappeared from the nasal secretion after treatment. Cases one, two, five, and seven showed partial or complete resolution of the specimen nodules examined after treatment.

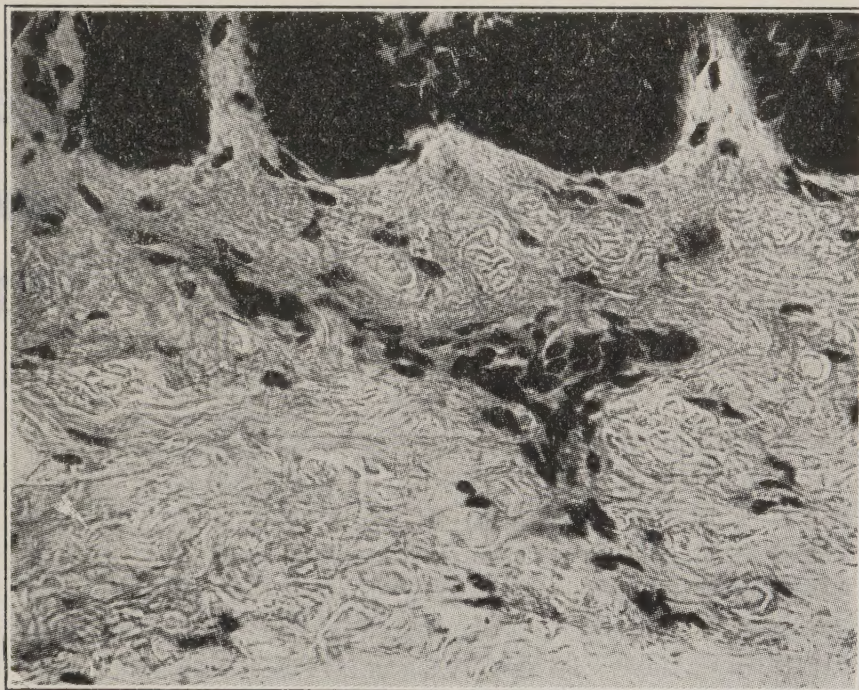


FIG. 12.—High magnification of Case 7; a few fibroblasts are seen.

In view of these experiments we can probably form the following opinions:

1. In cases where the patient is not too weak-

²The writer has not seen any of the cases for some months and cannot speak regarding their recent history.

Wellman: Salvarsan in Leprosy.

ened from the disease, salvarsan may be administered without harm.

2. Some improvement may be expected, especially in early cases.

3. We have no evidence that such effect of the drug is in any way specific or permanent.

4. "Arsenic has long been employed in leprosy," to quote from our preliminary note on this subject, "and we have no evidence that salvarsan is superior in its action to the other forms of arsenic which have been used by previous observers."

In conclusion the author wishes to acknowledge the help of Mr. Finley M. Eastman in the tiresome work of preparing the large number of specimens examined, and to thank Dr. M. Couret for making the photomicrographs accompanying this paper.

